Title: USE OF (4-ALKYLPIPERAZINYL)(PHENYL) METHANONES IN THE TREATMENT OF ALZHEIMER'S DISEASE

In the Claims

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1. (Previously Presented) A method for treatment of a mammal threatened or afflicted by Alzheimer's disease, by administering to said mammal an effective amount of a compound of formula I:

wherein:

- a) R^1 , R^2 and R^3 are individually H, OH, halo, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ alkoxy, $(C_3\text{-}C_6)$ cycloalkyl, $(C_3\text{-}C_6)$ cycloalkyl($(C_1\text{-}C_6)$ alkyl), $(C_2\text{-}C_6)$ alkenyl, $(C_2\text{-}C_6)$ alkynyl, $(C_1\text{-}C_6)$ alkanoyl, halo $(C_1\text{-}C_6)$ alkyl, hydroxy $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ alkoxycarbonyl, $(C_1\text{-}C_6)$ alkylthio, thio $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ alkanoyloxy, $N(R^6)(R^7)$ wherein R^6 and R^7 are individually H, O, $(C_1\text{-}C_6)$ alkyl, $(C_3\text{-}C_6)$ cycloalkyl, $(C_3\text{-}C_6)$ cycloalkyl, phenyl or benzyl, or R^6 and R^7 , together with the N to which they are attached form a 5- or 6-membered ring, optionally comprising 1-2 S, $N(R^6)$ or nonperoxide O, or R^1 and R^2 together are methylenedioxy;
- b) Y and Z together are =O, $-O(CH_2)_mO$ or $-(CH_2)_m$ wherein m is 2-4, or Y is H and Z is OR^9 or SR^9 , wherein R^9 is H or (C_1-C_4) alkyl:
- c) X is (C_1-C_6) alkyl, (C_1-C_6) alkoxy, hydroxyl (C_1-C_6) alkyl (C_3-C_{12}) alkenyl, (C_2-C_6) alkynyl, carboxy, (C_1-C_6) alkoxycarbonyl, thio (C_1-C_6) alkyl, (C_3-C_{12}) heterocycloalkyl (C_1-C_6) alkyl, aryl or heteroaryl, optionally substituted by 1, 2 or 3 \mathbb{R}^1 ; and the pharmaceutically acceptable salts thereof.
- 2. (Original) The method of claim 1 wherein the amount is effective to inhibit $A\beta$ peptide-induced neurotoxicity.
- 3. (Previously Presented) The method of claim 1 wherein the amount is effective to inhibit $A\beta_{1-42}$ neurotoxicity.

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4. (Previously Presented) The method of claim 1 wherein the amount is effective to inhibit glutamate-induced neurotoxicity in said mammal.

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- 5. (Previously Presented) The method of claim 1 wherein the amount is effective to maintain ATP levels in neuronal cells in said mammal.
- 6. (Original) The method of claim 5 wherein the cells are contacted in vitro.
- 7. (Original) The method of claim 5 wherein the cells are contacted in vivo.
- 8. (Previously Presented) The method of claim 1 wherein the compound of formula I is administered to a human.
- 9. (Original) The method of claim 8 wherein the human is in an early stage of AD.
- 10. (Original) The method of claim 8 wherein the human is an AD patient.
- 11. (Previously Presented) The method of claim 1 wherein R^1 , R^2 or R^3 is $N(R^6)(R^7)$.
- 12. (Previously Presented) The method of claim 1 wherein R^2 is (C_1-C_6) alkoxy.
- 13. (Previously Presented) The method of claim 1 wherein R^3 is (C_1-C_6) alkoxy.
- 14. (Previously Presented) The method of claim 1 wherein each of R^1 , R^2 and R^3 is (C_1 - C_3)alkoxy.
- 15. (Previously Presented) The method of claim 1 wherein Y and Z together are =0.

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- 16. (Previously Presented) The method of claim 1 wherein Y is H and Z is OH.
- 17. (Previously Presented) The method of claim 1 wherein X is (C_1-C_6) alkyl.
- 18. (Previously Presented) Method of claim 1 wherein X is CH₃.
- 19. (Previously Presented) The method of claim 1 wherein the compound of formula I is administered orally.
- 20. (Previously Presented) The method of claim 1 wherein the compound of formula I is administered parenterally.
- 21. (Previously Presented) The method of claim 1 wherein the compound of formula (I) is administered in combination with a pharmaceutically acceptable carrier.
- 22. (Original) The method of claim 21 wherein the carrier is a liquid, suspension or gel.
- 23. (Original) The method of claim 21 wherein the carrier is a solid.
- 24. (Previously Presented) The method of claim 1 wherein the compound of formula I is [(2,3,4-trimethoxy)phenyl]-[4-ethylpiperazin-1-yl] methanone.
- 25. (Original) A composition comprising a compound of formula (I) in combination with a pharmaceutically-acceptable carrier.
- 26. (Original) A therapeutic method to treat a neuropathy that involves a glutamate network or pathway hyperactivity comprising administering to a mammal threatened with, or afflicted by, said neuropathy, an effective amount of a compound of formula (I).

SUPPLEMENTAL PRELIMINARY AMENDMENT

Page 6 Docket No: 1941.001US1 Serial Number: 10/599,952 Docket |
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Title: USE OF (4-ALKYLPIPERAZINYL)(PHENYL) METHANONES IN THE TREATMENT OF ALZHEIMER'S DISEASE

27. (Canceled)